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**Histone demethylase LSD1 regulates neural stem cell proliferation.**

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**Public Summary:**

**Scientific Abstract:**

Lysine-specific demethylase 1 (LSD1) functions as a transcriptional coregulator by modulating histone methylation. Its role in neural stem cells has not been studied. We show here for the first time that LSD1 serves as a key regulator of neural stem cell proliferation. Inhibition of LSD1 activity or knockdown of LSD1 expression led to dramatically reduced neural stem cell proliferation. LSD1 is recruited by nuclear receptor TLX, an essential neural stem cell regulator, to the promoters of TLX target genes to repress the expression of these genes, which are known regulators of cell proliferation. The importance of LSD1 function in neural stem cells was further supported by the observation that intracranial viral transduction of the LSD1 small interfering RNA (siRNA) or intraperitoneal injection of the LSD1 inhibitors pargyline and tranylcypromine led to dramatically reduced neural progenitor proliferation in the hippocampal dentate gyri of wild-type adult mouse brains. However, knockout of TLX expression abolished the inhibitory effect of pargyline and tranylcypromine on neural progenitor proliferation, suggesting that TLX is critical for the LSD1 inhibitor effect. These findings revealed a novel role for LSD1 in neural stem cell proliferation and uncovered a mechanism for neural stem cell proliferation through recruitment of LSD1 to modulate TLX activity.

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